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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/540,843 | 05/18/2006 | Lorenza Mariscal-Gonzalez | UHT1.001APC | 2198 |

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| EXAMINER | |
|---|---|
| BLUMEL, BENJAMIN P | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 12/14/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/540,843 | MARISCAL-GONZALEZ ET AL. | |
| | Examiner | Art Unit | |
| | BENJAMIN P. BLUMEL | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *4/27/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *8-31 and 43* is/are pending in the application.

4a) Of the above claim(s) *10-15, 17-21 and 24-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,16,22,23,31 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/27/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 8, 9, 16, 22, 23, 31 and 43 are examined on the merits. Claims 10-15, 17-21 and 24-30 remain withdrawn from consideration as they are drawn to non elected species.

### *Response to Arguments*

Applicant's arguments with respect to claims 8, 9, 16, 22, 23, 31 and 43 have been considered but are moot in view of the new ground(s) of rejection.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**(New Rejection)** Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 recites, "…said composition is an oral dosage composition for intestinal delivery of the therapeutic agent and administering is by oral administration.", however, since the claim is reciting properties of a product and then requires an active step, it is unclear if the claimed invention is a product or a method.

***Claim Rejections - 35 USC § 102***

**(New Rejection)** Claims 8, 9, 16 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Potter et al. (US Pat. 5,422,110).

The claimed invention is drawn to a pharmaceutical composition for the delivery of a therapeutic agent that comprises the agent and an effective amount of a VP4 rotavirus protein or derived fusion proteins thereof. The therapeutic agent can be a peptide with biological activity and the composition is formulated for oral administration and contains a pharmaceutically acceptable vehicle.

Potter et al. teach the creation of a fusion protein based on the bacterial protein *leukotoxin* (a peptide with biological activity) and either somatostatin (SRIF), gonadotropin releasing hormone (GnRH) or rotavirus viral protein 4 (VP4). These fusion proteins are created through recombinant DNA techniques and are formulated for various routes of administration (i.e., oral, nasal, etc.) Moreover, for oral administrations, Potter et al. suggest using tablets, pills, and capsule, which would function as a pharmaceutically acceptable vehicle. Therefore, Potter et al. anticipated the claimed invention.

*See columns 2 (lines 37-62), 14-15 (abridging paragraph) and example 2.*

***Claim Rejections - 35 USC § 103***

**(New Rejection)** Claims 8, 9, 16, 22, 23, 31 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Langridge and Arakawa (US PGPub 2002/0055618 A1), Potter et al. (*supra*), and Honeyman et al. (Diabetes, 2000).

The claimed invention is drawn to a pharmaceutical composition for the delivery of a therapeutic agent that comprises the agent and an effective amount of a VP4 rotavirus protein or

derived fusion proteins thereof. The therapeutic agent can be a peptide with biological activity and the composition is formulated for oral administration and contains a pharmaceutically acceptable vehicle. The biologically active peptide can be a hormone (a therapeutic agent), such as insulin.

Langridge and Arakawa teach the formation of various fusion proteins that can contain different autoimmune autoantigens or pathogen autoantigens. Some examples are cholera toxin subunits, human insulin, rotavirus VP4, VP6, and shiga toxin. One specific example is the fusion of insulin to a cholera toxin subunit. Langridge and Arakawa teach that by administering such a fusion protein to a host, the onset of insulin-dependent diabetes mellitus (IDDM) can be mitigated. Langridge and Arakawa also teach that for oral administration, tablets can be used. However, Langridge and Arakawa do not specifically state that any pathogen autoantigen (i.e., rotavirus VP4) should be associated/linked to insulin. *See paragraphs 190 and 226-228 and example 1.*

The teachings of Potter et al. are discussed above, however, they do not teach the use of Insulin.

Honeyman et al. teach that in some instances, children infected by rotaviruses can develop type 1 diabetes and therefore require insulin supplementations over time. More specifically, Honeyman et al. report that rotaviruses contain certain epitopes that mimic that of the T-cell epitopes to self-antigens on the surface of Pancreatic Islet cells. Therefore, following exposure to rotaviruses, it is possible that circulating T-cells can then mistakenly target these islet cells. *See page 1319.*

It would have been obvious to one of ordinary skill in the art to modify the compositions taught by Langridge and Arakawa in order to use rotavirus VP4 and insulin in a fusion structure for oral administrations. One would have been motivated to do so, given the suggestion by Langridge and Arakawa that various combinations of antigens can be fused together. There would have been a reasonable expectation of success, given the knowledge that VP4 was previously used in a fusion protein with biological activity *in vivo*, as taught by Potter et al., and also given the knowledge that in certain documented rotavirus infections, IDDM onset is associated, as taught by Honeyman et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648